RESPONSE TO OFFICE ACTION

A. Status of the Claims

Claims 41-63 are presently pending, with claims 42, 46 and 61 withdrawn. Claim 41 is amended. Support for this amendment is found in the specification, for instance at p 49, line 20 through p 52, line 12 (Example 2). Claims 41, 43-45, 47-60, 62 and 63 are currently pending in the case and under consideration.

B. Rejection Under 35 U.S.C. § 112, First Paragraph – Written Description

The Action maintains the rejection of claims 41, 43-45, 47-60, 62 and 63 under 35 U.S.C. § 112, first paragraph, as allegedly lacking written description. In addition to the reasoning set forth in the previous Action, the present Action further asserts that the present specification fails to provide a representative number of species possessing common attributes or features to demonstrate that Applicants were in possession of the claimed genera of both pathogens and animals. Applicants respectfully traverse.

1. Claim Interpretation

Regarding the interpretation of the claims as set forth in the previous Action, Applicants note that its inaccuracy lies in the Action's apparent assertion that it is a *nucleic acid* that elicits an immune response, rather than an *antigen* encoded by a nucleic acid: for example, the Action states, "... and selecting and identifying the nucleic acid from the library that elicit[s] an immune response." Previous Action, point 10, p 5. However, the claimed method recites a method for identifying a nucleic acid from a library that codes for an *antigen* that elicits an immune response, and/or the encoded antigen. That is, the nucleic acid that elicits an immune response does so by being expressed in a subject to yield a protein or peptide antigen. *See* previous Response, pp 8-9. Further, the method comprises administration of either the identified nucleic acid or the antigen encoded by it, to a subject.

2. Genus of Pathogens

In contrast to the Action's assertion that the specification fails to provide a representative number of species of pathogens to satisfy the written description requirement, Applicants note that the specification informs one of skill in the art that ***any*** pathogen may be utilized in methods of the present invention. *See, e.g.*, p 5, lines 6-8 ("The invention, in general terms, arises from the inventors' success in developing a way to present to an animal a major number of antigenic determinants encoded by the genome of ***any*** pathogen." (emphasis added)). This is reiterated at p 5, line 29 through p 6, line 11, wherein numerous specific species are also provided:

> For example, the method has been applied to a mycoplasm, ***Mycoplasma pulmonis***, and to a eubacterium, ***Listeria monocytogenes***. These pathogens are but two examples of the wide range of pathogens that might be screened; the method is equally adaptable to screen for vaccines for ***HIV, malaria, mycoplasma, tuberculosis, respiratory syncytial virus, and conjugated pneumoccus; all pathogens for which there are no effective vaccines.*** One may also screen for alternative and improved vaccines for diseases such as smallpox and polio. Nor is the method limited necessarily to viruses and bacteria. ***Use of any pathogen is contemplated, including protozoa, yeast, fungi, worms or prions.*** It is only necessary to obtain genomic material e.g., DNA or RNA or, in the case of prions, because they are proteins, to isolate or synthesize a DNA that encodes the prion.

(emphases added). This section of the specification describes at least eight specific species of pathogens (*Mycoplasma pulmonis*, *Listeria monocytogenes*, HIV, malaria, mycoplasma, tuberculosis, respiratory syncytial virus, conjugated pneumoccus) and seven more general species of pathogens (viruses, bacteria, protozoa, yeast, fungi, worms, prions) that may be employed in the present invention. *See also* p 18, lines 6-9 (also listing algae and protozoa) and lines 24-30, including Table 1 (including the broad classes of *Mollicutes* and Gram-positive bacilli and the more specific species of *Rothia*, *kurthia* and *Oerskovia*). Taken together, at least ***twenty-two*** species of pathogens are set forth in the specification. Applicants respectfully note that if the Action has a basis for asserting that these twenty-two species do not constitute a

representative number of species within the claimed genus of pathogens, then the Action should be able to explain what number would be representative. No such basis or number has been provided.

Structural and functional features of the claimed pathogens are also disclosed. *See* MPEP § 2163 ("[T]he written description requirement for a claimed genus may be satisfied through sufficient description of a representative number of species by... disclosure of relevant, identifying characteristics, *i.e.*, structure or other physical... properties... or by a combination of such identifying characteristics, sufficient to show the application was in possession of the claimed genus.") One common structural attribute of the claimed pathogens is the presence of genomic material: "It is only necessary to obtain genomic material e.g., DNA or RNA or, in the case of prions, because they are proteins, to isolate or synthesize a DNA that encodes the prion." Specification, p 6, lines 9-11. This shared structural characteristic provides guidance to one of skill in the art as to which pathogens are contemplated by the present claims. Additionally, a discussion of the genomic size of a given pathogen also conveys possession of the claimed genus to one of skill in the art:

> Of course it is technically feasible to apply ELI to any pathogens with larger genomes. Genomes smaller than *Mycoplasm* and *Listeria*, many of which have genomes up to 100-fold smaller than *Mycoplasm*, are well-suited for application of the disclosed methods of identifying and isolating immunogens. These pathogens include HIV, known to have an exceptional number of variants and which is therefore an excellent candidate for screening with the ELI.

p 8, lines 4-9.

One functional aspect of pathogens of the present invention lies in the fact that the claimed DNA or RNA sequences that encode immune-responsive antigens are comprised in ***pathogens***, a recognized term of art. This term, by itself, conveys functional information. While the mechanisms of action of different pathogens may differ, one advantage of the present

invention lies in the applicability of the claimed methods to a wide variety of pathogens: "The new ELI method combines the advantages of genetic immunization ***without the necessity of discovering a single protective gene or foreknowledge of the pathogen's biology***." Specification, p 8, lines 14-16 (emphasis added); *see also* p 17, lines 25-29 ("The method operates on the assumption, generally accepted by those skilled in the art, that all the potential antigenic determinants of any pathogen are encoded in its genome."). By restricting the types of biological agents that may be employed in methods of the present invention to pathogens, the claims and specification convey a functional aspect of the claimed genus to a person of skill in the art in a manner that satisfies the written description requirement.

In view of the disclosure in the specification and knowledge of one skilled in the art, therefore, the claimed genus of pathogens is adequately supported. MPEP § 2163 (II)(3)(a)(ii); *In re Rasmussen*, 650 F.2d 1212, 1214, 211 USPQ 323, 326-27 (CCPA 1981).

3. Genus of Animals

The Action asserts that the present specification fails to provide adequate written description for the genus of claimed animals, stating, "only one species (mouse) of the claimed genus of subjects is disclosed by the instant specification." Action, p 5. Applicants respectfully note that, in addition to the working examples that discuss mice, other species are also disclosed throughout the specification. *See, e.g.*, p 8, lines 18-19 (mammals); p 11, lines 21-22 and p 26, lines 6-9 (humans); p 49, line 29 through p 50, line 2 (rodents). If the Action has a basis for asserting that these disclosed species do not constitute a representative number of species within the claimed genus of subjects, then the Action should be able to explain what number would be representative. No such basis or number has been provided. Further, if the Action's basis for the rejection lies in the discussion of only mice in the working examples, the MPEP clearly states

that working examples are not needed to satisfy the written description requirement. MPEP § 2163 (II)(A)(3)(a). As such, the claimed genus of subjects is adequately supported.

4. Conclusion

In view of the above, the claimed genus of pathogens and the claimed genus of animals are each adequately supported in a manner that satisfies the written description requirement. Withdrawal of the rejection is therefore respectfully requested.

C. Rejection For Non-Statutory Double Patenting

Three separate obviousness-type double patent rejections have been issued over U.S. Application Serial No. 10/023,437, U.S. Patent No. 5,703,057 and U.S. Patent No. 6,410,241, respectively. While the Action recognizes Applicant's statement regarding the filing of terminal disclaimers with respect to the '437 Application and the '057 Patent, the Action continues to maintain the obviousness-type double patenting rejection of claims 41, 43, 59-60, 62 and 63 over claims 1-28 of the '241 Patent. Applicants generally traverse, but note that a terminal disclaimer will be submitted upon indication of allowable subject matter.

D. Rejections Under 35 U.S.C. § 102

(1) The Action again rejects claims 41, 43-45, 47-50, 54-56, 59 and 62 as allegedly anticipated under 35 U.S.C. § 102(b) by Lai *et al.* (*Vaccine.* Vol. 12:291-298; March, 1994). In addition to reasoning set forth in the previous Action, the present Action asserts that the third selection step of part (a) of claim 41 does not require the procedure to be carried out *in vivo*. As such, it is alleged that not all of the sub-steps of part (a) need to be performed *in vivo*.

Applicants traverse, and note that claim 41 reads as follows:

> 1. A method of vaccinating a subject comprising:
> (a) obtaining a nucleic acid encoding an antigen or an antigen that is encoded by said nucleic acid, wherein the nucleic acid or antigen has been determined to elicit an immune response by a method comprising

the steps of:

i) obtaining a library comprising DNA or RNA sequences from a pathogen;
ii) introducing a plurality of members of said library into an animal; and
iii) performing *in vivo* selection of at least a first member from the library that elicits an immune response to identify said nucleic acid or antigen; and

(b) administering the nucleic acid or antigen to a subject in a manner effective to vaccinate the subject against the pathogen.

As noted in the previous Response, Lai *et al.* screened their genetic library *in vitro* (*see e.g.*, p. 294 col. 1). Constructs (library members) that had been pre-selected based on the *in vitro* immunological screen were then introduced into an animal to study their immunogenicity. Thus, Lai *et al.* in no way teach the method of claim 1, in which the screen (claim 1, step (a)) is carried out *in vivo*. Applicants therefore respectfully request that the anticipation rejection be withdrawn.

(2) The Action again rejects claims 41, 45, 47, 48, 59, 60 and 62 under 35 U.S.C. § 102(a) as anticipated by Coney *et al.* (*Vaccine.* Vol. 12:1545-1550, 12/1994). The Action bases the rejection, in part, on the assertion that the present claims encompass an *in vitro* selection step. Applicants respectfully traverse.

As noted above, claim 41, part (a), step (iii) recites an *in vivo* selection step. Coney *et al.*'s method of screening for immunogenicity is not described to occur via a method of *in vivo* screening of a plurality of genetic library members. For at least this reason, the present claims are not anticipated, and withdrawal of the rejection is thus respectfully requested.

E. Rejection Under 35 U.S.C. § 103(a)

The Action again rejects claims 41, 43-45, 47-60, 62 and 63 under 35 U.S.C. § 103(a) as obvious over Lai *et al.* in view of Felgner *et al.* (U.S. Patent No. 5,589,466). The Action bases the rejection, in part, on the assertion that Lai *et al.* teaches all of the steps of the claimed method.

In response, Applicants traverse and note that, as described above, Lai *et al.* do not describe *in vivo* screening of a library of DNA constructs. Felgner *et al.* likewise do not describe such a method. Rather, they describe delivering an isolated polynucleotide (*e.g.*, abstract, line 1) to exert a therapeutic effect. Each example that describes administration of a polynucleotide does so with respect to a specific coding sequence, such as a CAT gene, or a dystrophin gene. This is in contrast to the presently claimed method, in which the polynucleotide(s) screened in step (a) of claim 1 is not isolated or identified prior to the screening step, but is among a plurality of library members. As each of the cited references do not teach every element of the claims, the teachings of Lai *et al.*, in view of Felgner *et al.*, do not render the present claims obvious. *See* MPEP § 2142. Withdrawal of the rejection is thus respectfully requested.

CONCLUSION

This is submitted to be a complete response to the referenced Office Action. In conclusion, Applicant submits that, in light of the foregoing remarks, the present case is in condition for allowance and such favorable action is respectfully requested.

The Examiner is invited to contact the undersigned at (512) 536-3015 with any questions, comments or suggestions relating to the referenced patent application.

Respectfully submitted,

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